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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,594	11/14/2003	Mohamed Attawia	3518.1012-005	3230

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EXAMINER	
STANDLEY, STEVEN H	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,594	ATTAWIA ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2006*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-18,20-24 and 27-31* is/are pending in the application.

4a) Of the above claim(s) *27-30 are withdrawn* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 10-18, 20-24, and 31-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 12/11/06 has been made of record. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Priority

2. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/456,948, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The Examiner has considered Applicant's arguments concerning priority and finds that while application 10/456,948 contains prophetic teachings of treatment with mesenchymal cells, the prior art cited (Sakai et al., 2003) in rejections under both 35 USC § 112, 1st paragraph, and 35 USC § 103 provides the only enabled aspects of the instant invention. In other words, the claims are only enabled to the extent that the prior art teaches the instant invention. Thus, the earliest time

at which the invention can be considered enabled by the prior art is at application 10/714,559, filed 11/13/03.

Objections/Rejections: Withdrawn

Claim Rejections - 35 USC § 112

3. Rejection of claims 1-7, 10-18, 20-24, and 31-32 under 35 USC § 112, 1st, written description, is withdrawn due to applicant's amendment.

4. Rejection of claim 24 under 35 USC § 112, 2nd paragraph, is withdrawn due to applicant's amendment.

Objections/Rejections: Maintained/New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Rejection of claim 1-7, 10-18, 20-24, and 31-32 under 35 USC § 112, 1st paragraph, enablement is maintained for the reasons made of record in the office action dated 9/17/06. Applicant's arguments have been fully considered and not found to be persuasive. Applicant argues first that amendment from 'autologous

cells' to 'mesenchymal cells' in claim 1 obviates the rejection. This is not persuasive because many of the other limitations outside the scope of enablement are not included in base claim 1 or any other claims. Applicant next argues that inclusion in claim 7 of a therapeutic agent which is a growth factor, and the recitation of TGF-Beta in claim 18 obviates the rejection. This is not found persuasive because some growth factors actually inhibit proliferation of chondrocytes, which would destroy the instant invention. For instance, both NGF and bFGF inhibit proliferation of chondrocytes both in vitro and in vivo (see Raucci et al, 2004). Thus, the method would not work with a generic growth factor. Applicant lastly argues on page 9 of Remarks that a carrier medium that does not cause retention of mesenchymal cells at the site of placement is useful. Since applicant is treating a degenerative disc disease, retention of mesenchymal cells at the locus of repair is an essential property. Moreover, Hyaluronan was found to be toxic to the cells at 15%. See Crevensten et al, page 433, right column.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Rejection of claims 1-3, 5-6, 10-16, 20-24 and 31 under 35 USC § 103(a) is maintained for the reasons made of record in the office action dated 9/17/06. Applicant's arguments have been fully considered and not found to be persuasive. Applicant argues first that Sakai et al was published in September of 2003 and is thus not available as prior art. This is not found persuasive because the invention as claimed is not enabled prior to the publication of Sakai et al. Thus, it is not entitled to priority to the continuations in part as argued by applicant. Furthermore, the earliest publication of Sakai et al is as an abstract from the annual meeting of the international society for the study of lumbar spine (May, 2003). Applicant argues secondly that one of ordinary skill in the art would not be motivated to practice the claimed invention with a reasonable expectation of success based on the teachings of Sakai et al. This is not found persuasive because Sakai, in fact, practices a more difficult method in culturing mesenchymal cells in order to label them, but also in order to expand them, because Sakai et al demonstrate the viability of the cells after two weeks of culturing.

The motivation to concentrate and administer mesenchymal stem cells is that the procedure would take hours instead days. The expectation of success is, indeed, higher than that demonstrated by Sakai et al because there is less opportunity for contamination in a period of hours instead of days or weeks.

Applicant argues that the method of Sakai et al cannot be used as a therapeutic. This is not found persuasive because Sakai et al demonstrate the effectiveness of the treatment (see abstract of publication, or 'results' section of the annual meeting abstract (submitted in applicant's ids).

Applicant also argues on page 12 of Remarks that Sakai's culturing of stem cells would not be a desirable treatment because of the size of the resulting population would be too large. This is not persuasive because the method of Sakai et al is effective. The specification has not distinguished the method in any non-obvious sense from that of Sakai. Sakai et al has constructed the method in order to overcome the burden of proof that the cells are viable and alive and integrate into their environment. To do this, Sakai et al must culture them and label them with a fluorescent marker, which then facilitates identification of new cells that have integrated into the area. Sakai et al demonstrate that the instant method would obviously work, and do it prior to the priority of the instant application.

7. Claims 1-6,10-16, 20-24, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al as applied to claims 1-3, 5-6, 10-16, 20-24, and 31 above, and further in view of Tanney et al (1980).

Sakai et al teaches as described above.

Sakai et al does not teach concentrating cells by filtration.

Tanney teaches concentrating cells by a filtration technique (see abstract).

One would have every expectation of success since the technique uses a 0.2 micrometer size exclusion pore that captures things over 0.2 micrometers and allows smaller things to pass.

One would be motivated to combine the references because the method of Tanney provides an easy way to concentrate cells with no impairment of organism viability (see abstract).

7. Claims 1-3, 5-7,10-16, 18, 20-24, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al as applied to claims 1-3, 5-6, 10-16, 20-24, and 31 above, and further in view of Russell et al (may 2003 meeting abstract, in applicant's IDS).

Sakai teaches as described above.

Russell et al teach that bone marrow mesenchymal stem cells can be used as a source for treatment of disc degeneration as Sakai et al does. In addition, Russell et al teach using TGF-beta to stimulate chondrocyte differentiation (see results and discussion).

One of ordinary skill in the art would be motivated to combine the two references because tgf-beta stimulated mesenchymal cells were stimulated to differentiate into chondrocytic phenotype is critical to mimic disc like-cells.

The expectation of success is high because the instant invention uses the same tgf-beta with the same cell type for the same treatment.

8. Claims 1-3, 5-7,10-17, 18, 20-24, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakai et al as applied to claims 1-3, 5-

6, 10-16, 20-24, and 31 above, and further in view of Russell et al (may 2003 meeting abstract, in applicant's IDS).

Sakai et al and Russell et al teach as described above.

Sakai et al. and Russell et al do not teach a carrier comprised of microspheres.

However, carriers such as microspheres are will-known in the art, would have a reasonable expectation of success, and one would be motivated to use them because they would provide solid support for holding cells in the locus of delivery.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven H. Standley whose telephone number is (571) 272-3432. The examiner can normally be reached on 8:00-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Janet Andre can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Steven Standley, Ph.D.

7/21/05

Donna Ramos
PRIMARY EXAMINER